



Title: CLONING, SEQUENCING AND CHARACTERIZATION  
 OF TWO CELL DEATH GENES AND USES THEREFOR  
 Applicant (s): H. Robert Horvitz et al.  
 Serial No.: 08/984,178  
 Filing Date: December 3, 1997  
 Customer No.: 21559  
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## FIG. 1A

GAATTCCGCGTCGAATCATTGTCTGTTGGTATCGATTCAAGAACCGAAACTTGTGATCGA  
 1 +-----+-----+-----+-----+-----+-----+-----+-----+-----+ 60  
 TAACAAGTCATTCAAACACGGCGAAGATGTCTATCGTATAACAGAATATTGGAGAAAT  
 61 +-----+-----+-----+-----+-----+-----+-----+-----+-----+ 120  
 GCTCGCAAAACTCGAAATTGTCAACGATAAAATGATTAACCTGAAGGGGCTAATGTAAGT  
 121 +-----+-----+-----+-----+-----+-----+-----+-----+-----+ 180  
 TATCTGATGTTCTACAATTAAAAAAATTGTTTTTTCCAAATTAAATTTCGAAGATT  
 181 +-----+-----+-----+-----+-----+-----+-----+-----+-----+ 240  
 AACGAAAACGATTAAAATCAATAAAACGCAATAAAGAGGGCTGGCTTCTTTAAT  
 241 +-----+-----+-----+-----+-----+-----+-----+-----+-----+ 300  
 TTAAATTATAATTTCGATTGTTGTATGAAGCTACAAATGTACTGTTTGATTTG  
 301 +-----+-----+-----+-----+-----+-----+-----+-----+-----+ 360  
 AATATTGTATTACAGGGTTGGGATTCTCGCAAATATCAGCGACAGTGGAAAGATTTAGAA  
 361 +-----+-----+-----+-----+-----+-----+-----+-----+-----+ 420  
 GAAGGACGTGTGACAATCACTAAGTCAAAGAGGGAAAGGATAAAGGATTGTGATATTCA  
 421 +-----+-----+-----+-----+-----+-----+-----+-----+-----+ 480  
 CTGTTTACTCATCGCTTTAAATAAGAACTATATGCCGATTGCCGATATATTTCG  
 481 +-----+-----+-----+-----+-----+-----+-----+-----+-----+ 540  
 TTTATTAGGCCTCTCACATTCTGTACAATGTTCTACAAATAACTGCATTTATCT  
 541 +-----+-----+-----+-----+-----+-----+-----+-----+-----+ 600  
 GAAAATTGAAATTATTTTGCTACTTTTACTCGTTGCATCGAGATCAGCATATCTT  
 601 +-----+-----+-----+-----+-----+-----+-----+-----+-----+ 660  
 CCGGTCTATTATATTCAACGATTTATAAATTAGTACTCCTTCATGTTAATTTCATT  
 661 +-----+-----+-----+-----+-----+-----+-----+-----+-----+ 720  
 TTATCTGTAAGCTTACTGTATTTTTAAATCTTCTGCTTCTATCTGATTACAA  
 721 +-----+-----+-----+-----+-----+-----+-----+-----+-----+ 780  
 TGTTCTTACTCATTTCAAGGTATTTTATGCCCTCACAAATTATGCACATTCGGGCTT  
 781 +-----+-----+-----+-----+-----+-----+-----+-----+-----+ 840  
 GGAGATTATCCTCTATATTACATGCCGTTTTAAAGGATATAATGTTAACAAATA  
 841 +-----+-----+-----+-----+-----+-----+-----+-----+-----+ 900  
 ATTTTTATCAATGCTATTGTATATTCTCCAGCTAACCGTTGGCGAAACATCACCTA  
 901 +-----+-----+-----+-----+-----+-----+-----+-----+-----+ 960  
 GCATTTAAAATTCACAAATCTGCTCCTATAATCAAGAAGATTTTCAGATGCTCT  
 961 +-----+-----+-----+-----+-----+-----+-----+-----+-----+ 1020  
 M L C  
 1↓  
 GCGAAATCGAATGCCCGCTTGAGCACGGCACACACGAGGCTCATCCACGACTTGAAC  
 1021 +-----+-----+-----+-----+-----+-----+-----+-----+-----+ 1080  
 E I E C R A L S T A H T R L I H D F E P  
 10 20  
 T n1162  
 ↑  
 CACGTGACGCATTGACTTATTTAGAAGGAAAAACATTTCACAGAAGATCATTCTGAAC  
 1081 +-----+-----+-----+-----+-----+-----+-----+-----+-----+ 1140  
 R D A L T Y L E G K N I F T E D H S E L  
 30 40  
 TTATCAGTAAAATGTCAACTGCCCTCGAGAGGATGCCAATTTCTCGAATCTATCGAC  
 1141 +-----+-----+-----+-----+-----+-----+-----+-----+-----+ 1200  
 I S K M S T R L E R I A N F L R I Y R R  
 50 60  
 GTCAAGCTTCTGAACCTGGACCACTCATGACTTTCAACTACAACAATCAAAGTCACC  
 1201 +-----+-----+-----+-----+-----+-----+-----+-----+-----+ 1260  
 Q A S E L G P L I D F F N Y N N Q S H L  
 70 80



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FIG. 1B

TTGCTGATTCCCTCGAAGACTACATCGATTTGCGATAAAATGAGCCAGATCTACTTCGTC  
1261 A D F L E D Y I D F A I N E P D L L R P + 1320  
90 100

CA GTAGT GATT GCT CCACA ATTT CCCGACAAATGCTCGATAGGAAACTATTGCTTGGGA  
1321 V V I A P Q F S R Q M L D R K L L G N + 1380  
110 120  
T n2274 ↑  
ATGTTCCAAAACAAATGACATGCTATATTGAGAGTATCAGTGGATCGAGTGATCAAAA  
1381 V P K Q M T C Y I R E Y H V D R V I K K + 1440  
130 140

Intron 1  
AGCTCGACGAGATGTGTGATTTAGGTGAGAAA ACTGGAAAGCTCTCGTGTATTATAATC  
1441 L D E M C D L D + 1500  
TTGCTTAAACTTCAGACTCCTTTCTGTTCTACACGGCCGAGCTGGATCCGGAAAAT  
1501 S F F L F L H G R A G S G K S + 1560  
160

Intron 2  
CAGTAATTGCATCACAGCTTTGAAATCTGACCAACTTATTGGAATGTGAGTGGTAT  
1561 V I A S Q A L S K S D Q L I G I + 1620  
170 180

TATCTGAATCTACGGATCTCATTCTATTACAGAAATTATGATTCAATCGTTGGCTCAA  
1621 N Y D S I V W L K + 1680  
190

AGATAGTGGAACAGCTCCAAAATCTACATTGATTATTTACGGATATTTGCTGATGCT  
1681 D S G T A P K S T F D L F T D I L L M L + 1740  
200 210

A n1920/n2247  
↑ Intron 3  
AAAGTGAGTGAATAGAGTGCATGTAACATTGAGCATGATTGAAATTATGAAAATTGAA  
1741 K + 1800

CCTGGTTAGCTTTAATTGATATTCGTGACGCTTGCATGTTGTGTGTTGAAGACG  
1801 AGCCCGTGTGAGCGACACGGATGACTCGATTGACCTAACCGACTTCAATTACCGTGT  
1861 A n2273 ↑  
TCTTTCAAGAAGCGAAGACGATCTCTCAATTCCCACGGTGGAGCATGTCACGTCAGT  
1921 S E D D L L N F P S V E H V T S V + 1980  
220



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## FIG. 1C

## Intron 4

1981 TGTACTCAAAGGATGGTAAGTTGCCGATTCTGGTACAATATCTTAAATTATTGGT 2040  
 V L K R M

2041 TTTTAGATCTGCAACGCACTCATTGATCGTCAAATACTTATTGTATTGATGACGTA 2100  
 I C N A L I D R P N T L F V F D D V  
 240 A n1948 T n1947 250  
 ↑ ↑  
 GTTCAAGAAGAAACAATTCTGGCTCAGGAGCTACGTCTCGATGTCTGTAACTACT 2160  
 2101 V Q E E T I R W A Q E L R L R C L V T T  
 260 270  
 CGTGACGTGGAAATATCAAATGCTGCTCTCAAACATGCGAATTGAAAGTGACATCA 2220  
 2161 R D V E I S N A A S Q T C E F I E V T S  
 280 290  
 TTGGAAATCGATGAATGTTATGATTCTAGAACGCTTATGGAATGCCATGCCTGTTGGA 2280  
 2221 L E I D E C Y D F L E A Y G M P M P V G  
 300 310  
 Tc4 n1416  
 ↓  
 GAAAAAGAAGATGTGCTTAATAAAACAATCGAACTAACAGCAGTGGAAATCCAGCAACG 2340  
 2281 E K E E D V L N K T I E L S S G N P A T  
 320 330  
 Intron 5  
 2341 CTTATGATTTTCAGTCTTGTGAACCGAAAACATTGAAAAGTGAGTGGACATACC 2400  
 L M M F F K S C E P K T F E K  
 330  
 AATTTGAGACTTTAAAATAATTCTACAATAAAAGTTAATCAAAAGTTCATAGC 2460  
 2401 TGATTGTCTTAAATTAGAATTGAGGATCAAAATCAAGAATTAGGATCCTGGCACGA 2520  
 2461 GAGAAAATGTGTAGCTACCGTACCCGAGAGATTCTTGATATTGCCATCGATTAAAT 2580  
 2520 TTTTTAAGAAAATTATCGTTTACATAATTGAACAAGAGATAACCGGTCTGACCCGACG 2640  
 2581 GAAATTTTAAATGAAAGCGAGTATGAGCCTGTTCAATTATTTGATTTCTCTTG 2700  
 2641 TTGTTCTTTTATTAAAGCCTTTATTGAAACAAGTCAAAATATTAAAAACTGA 2760  
 2701 ATAAAATATTAAAAAAATCAAGTAAATAGAAAAACAGCAAGGCTGGAGACTACTGTA 2820  
 2760 CTTCTAAATCCGCATACTCTTTATTAAATCATTTCCGAATGTCGAAACGAAATAA 2880  
 2821 TACATTTAGTCCAAATCGCTAGGTATATTCTAAAATTATCAAACATTTGCATTCA

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FIG. 1E

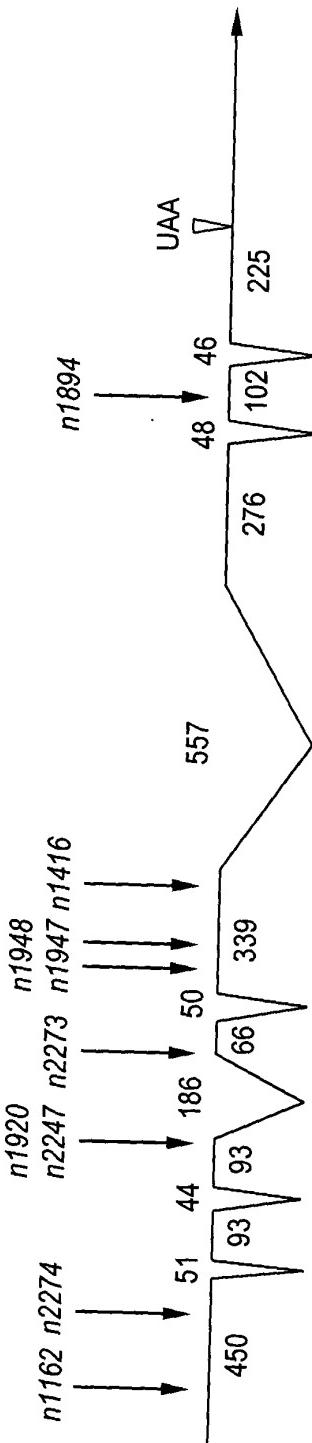
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FIG. 2





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## FIG. 3

	10	12	14		18	21
	X	Y	Z		-X	-Z
	D	N	S		T	E
Calcium-binding loop consensus		D	N		S	
			D		E	
					Q	
					D	
					N	
EF-hand consensus	O	*	O	G	*	*
ced-4 sequence 1	<u>Y</u>	N	<u>N</u>	<u>Q</u>	<u>S</u>	<u>H</u>
sequence 2	<u>S</u>	<u>L</u>	<u>E</u>	<u>I</u>	<u>D</u>	<u>E</u>
Parvalbumin (carp)	D	Q	D	K	<u>S</u>	<u>G</u>
(hake)	D	Q	D	K	<u>D</u>	<u>D</u>
(ray)	D	S	D	G	<u>D</u>	<u>H</u>
SCBP ( <i>Amphioxus I</i> )	D	I	N	K	<u>D</u>	<u>D</u>
ICaBP (bovine)	A	K	<u>E</u>	G	<u>D</u>	<u>P</u>
	D	K	<u>N</u>	G	<u>D</u>	<u>G</u>
Troponin C (rabbit)	D	A	D	G	<u>G</u>	<u>G</u>
	D	E	D	G	<u>S</u>	<u>G</u>
	D	R	N	A	<u>D</u>	<u>G</u>
Calmodulin (bovine)	D	K	D	G	<u>N</u>	<u>G</u>
Trypsinogen	L	G	<u>E</u>	D	<u>N</u>	<u>I</u>
Fibrinogen	D	N	D	N	<u>D</u>	<u>K</u>
Villin	G	V	D	P	<u>S</u>	<u>R</u>
GBP	D	L	N	K	<u>D</u>	<u>G</u>
					Q	I
					<u>Q</u>	<u>I</u>
					<u>Q</u>	<u>I</u>
					<u>Q</u>	<u>I</u>



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FIG. 4A

### **ced-3 Genomic Sequence**

AGATCTGAAATAAGGTATAAATTATAAGTGTATTCGAGGAAATTGACTGT  
1 -----+-----+-----+-----+-----+-----+-----+ 60  
TTAGCACAATTAAATCTGTTCAAGAAAAAGTCCAGTTCTAGATTTCCGTCTTA  
61 -----+-----+-----+-----+-----+-----+-----+ 120  
TTGTCGAATTAATATCCCTATTATCACTTTCATGCTCATCCTCGAGCGGCACGTCC  
121 -----+-----+-----+-----+-----+-----+-----+ 180  
AAAGAATTGTGAGAGCAAACGCGCTCCATTGACCTCCACACTCAGCCGCAAACAAAC  
181 -----+-----+-----+-----+-----+-----+-----+ 240  
GTTCGAACATTCTCGTGTGTTGCTCCTTTCCGTTATCTTGAGTCATCTTGTGCGTT  
241 -----+-----+-----+-----+-----+-----+-----+ 300  
TTTCTTGTCTTTGTTGAACGTGGCTAAGCAATTATTACATCAATTGAAGAAAA  
301 -----+-----+-----+-----+-----+-----+-----+ 360  
GGCTCGCCGATTATTGTTGCCAGAAAGATTCTGAGATTCTCGAAGTCGATTATAATA  
361 -----+-----+-----+-----+-----+-----+-----+ 420  
TTAACCTGGTTTGCAATTGTTCTAAAAAACCACTGTTATGTGAAAACGAT  
421 -----+-----+-----+-----+-----+-----+-----+ 480  
TAGTTACTAATAAAACTACTTTAACCTTACCTTACCTCACCGCTCCGTGTTCATG  
481 -----+-----+-----+-----+-----+-----+-----+ 540  
GCTCATAGATTTCGATACTCAAATCBBBBAAATTACGAGGGCAATTATGTGAAA  
541 -----+-----+-----+-----+-----+-----+-----+ 600  
CAAAAACAATCCTAACAGATTCCACATGTTGACCTCTCCGGCACCTCTCCTTAGCCCC  
601 -----+-----+-----+-----+-----+-----+-----+ 660  
ACCACTCCATCACCTTTGGCGGTGTTCTCGAAACCACTTAGGAAAGCAGTGTGAT  
661 -----+-----+-----+-----+-----+-----+-----+ 720  
CTCATTTGGTATGCTTTGATTTATAGCTCTTGTGCAATTCAATGCTTAAAC  
721 -----+-----+-----+-----+-----+-----+-----+ 780  
AATCCAAATCGCATTATATTGTGCATGGAGGCAAATGACGGGTTGGAATCTTAGATGA  
781 -----+-----+-----+-----+-----+-----+-----+ 840  
GATCAGGAGCTTCAGGGTAAACGCCGGTCACTTGTACCACTTCACTCATTTCCT  
841 -----+-----+-----+-----+-----+-----+-----+ 900  
GTCGTCCTGGTATCCTCAACTTGTCCCGGTTTGTGCGTACACTCTCCGTGATGC  
901 -----+-----+-----+-----+-----+-----+-----+ 960  
CACCTGTCTCCGTCATTAGAAATGTGAACTGTCCAGATGGGTGACTCATA  
961 -----+-----+-----+-----+-----+-----+-----+ 1020  
TTGCTGCTGCTACAATCCACTTCTTCTCATCGGCAGTCTTACGAGCCCACATAAAC  
1021 -----+-----+-----+-----+-----+-----+-----+ 1080  
TTTTTTCCGCAAATTGCAATAAACCGGCCAAAACCTCTCAAATTGTTACGCAA  
1081 -----+-----+-----+-----+-----+-----+-----+ 1140  
TATATACAATCCATAAGAATATCTCTCAATGTTATGATTCTCGCAGCAGTCTCT  
1141 -----+-----+-----+-----+-----+-----+-----+ 1200  
TCGTGTGCTAACATCTTATTTTATAATTCCGCTAAAATCCGATTGGTATTGAGTATTA  
1201 -----+-----+-----+-----+-----+-----+-----+ 1260  
ATTTATCGTAAAATTATCATAATAGCACCGAAAACACTAAATGGTAAAAGCTCCTT  
1261 -----+-----+-----+-----+-----+-----+-----+ 1320

### Repeat 1

TAAATCGGCTCGACATTATCGTATTAAGGAATCACAAAATTCTGAGAATGCGTACTGC  
1321 -----+-----+-----+-----+-----+-----+-----+ 1380  
  
- - - - -  
AACATATTTGACGGCAAAATATCTCGTAGCGAAAACATACAGTAATTCTTTAAATGACTAC  
1381 -----+-----+-----+-----+-----+-----+-----+ 1440



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## FIG. 4B

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Repeat 1

```

-----> -----<
TGTAGCGCTTGTGTCGATTTACGGGCTCAATTTTGAAAATAATTTTTTTCGAATT
1441 -----+-----+-----+-----+-----+-----+-----+-----+ 1500

-----<
TGATAACCCGTAAATCGTCACAACGCTACAGTAGTCATTTAAAGGATTACTGTAGTTCTA
1501 -----+-----+-----+-----+-----+-----+-----+-----+ 1560

-----<
GCTACGAGATATTTGCGCGCCAAATATGACTGTAATACGCATTCTCTGAATTTGTGTT
1561 -----+-----+-----+-----+-----+-----+-----+-----+ 1620
TCCGTATAATTCACAAGATTTGGCATTCCACTTAAAGGCGCACAGGATTATTCCA
1621 -----+-----+-----+-----+-----+-----+-----+-----+ 1680
ATGGGTCTCGGCACGCAAAAGTTGATAGACTTTAAATTCTCCTTGCATTTAAC
1681 -----+-----+-----+-----+-----+-----+-----+-----+ 1740
AATTACTAAAATTCGTGAATTTCTGTTAAAATTTAAAATCAGTTTCTAATATT
1741 -----+-----+-----+-----+-----+-----+-----+-----+ 1800
TTCCAGGCTGACAAACAGAAACAAAAACACAACAAACATTAAAAATCAGTTTCAAAT
1801 -----+-----+-----+-----+-----+-----+-----+-----+ 1860
TAAAAATAACGATTCTCATCGAAAATTGTGTTTATGTTGCGAAAATAAAAGAGAACT
1861 -----+-----+-----+-----+-----+-----+-----+-----+ 1920
GATTCAAAACAATTAAACAAAAAAACCCCCAAATCGCCAGAAATCAAGATAAAAAAA
1921 -----+-----+-----+-----+-----+-----+-----+-----+ 1980
TTCAAGAGGGTCAAAATTCCGATTTACTGACTTCACCTTTTTCGTAGTTCACT
1981 -----+-----+-----+-----+-----+-----+-----+-----+ 2040
GCAGTTGTTGGAGTTTGACGAAAATAGGAAAAAAATCGATAAAAATTACTCAAATCG
2041 -----+-----+-----+-----+-----+-----+-----+-----+ 2100
AGCTGAATTTGAGGACAATGTTAAAAAAAAACACTATTTCCAATAATTCACCAT
2101 -----+-----+-----+-----+-----+-----+-----+-----+ 2160

-----<
TTTCAGACTAAATCGAAAATCAAATCGTACTCTGACTACGGGTCAGTAGAGAGGTCAACC
2161 -----+-----+-----+-----+-----+-----+-----+-----+ 2220

-----<
ATCAGCCGAAGATGATGCGTCAAGATAGAAGGAGCTTGCTAGAGAGGAACATTATGATGT
2221 -----+-----+-----+-----+-----+-----+-----+-----+ 2280
M M R Q D R R S L L E R N I M M F
1 10
T (n1040)
|
TCTCTAGTCATCTAAAGTCGATGAAATTCTCGAAGTTCTCATCGAAAACAAGTGTGA
2281 -----+-----+-----+-----+-----+-----+-----+-----+ 2340
S S H L K V D E I L E V L I A K Q V L N
20 30
| Intron 1
ATAGTGATAATGGAGATATGATTAATGTGAGTTTAATCGAATAATAATTTAAAAAAAA
2341 -----+-----+-----+-----+-----+-----+-----+-----+ 2400
S D N G D M I N
40

```



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## FIG. 4C

AATTGATAATATAAAGAATATTTTGCACTCATGTGGAACGGTCGCGAGAAGAGACGGG  
 2401 -----+-----+-----+-----+-----+-----+ 2460  
 S C G T V R E K R R E  
 50  
 A (n718)

AGATCGTAAAGCAGTGCAACGACGGGAGATGTGGCGTTGACGCCTTATGATGCTC  
 2461 -----+-----+-----+-----+-----+-----+ 2520  
 I V K A V Q R R G D V A F D A F Y D A L  
 60 70  
 | Intron 2  
 TTCGCTCTACGGGACACGAAGGACTTGCTGAAGTCTTGAACCTCTGCCAGATCGTAGG  
 2521 -----+-----+-----+-----+-----+-----+ 2580  
 R S T G H E G L A E V L E P L A R S  
 80 90

TTTTAAAGTCGGCGAAAAGCAAGGGCTCACGGAAAAAGAGGCGGATCGTAATTT  
 2581 -----+-----+-----+-----+-----+-----+ 2640  
 GCAACCCACCGGCACGGTTTTCTCCGAAATCGGAAATTATGCACTTCCAAATAT  
 2641 -----+-----+-----+-----+-----+-----+ 2700  
 TTGAAGTGAATATATTTTACTGAAAGCTCGAGTGATTATTTATTAAACACTA  
 2701 -----+-----+-----+-----+-----+-----+ 2760  
 ATTTCTGGCGAAAAGGCCATTTGTAGATTGCCGAAATCTTGTACACACACAC  
 2761 -----+-----+-----+-----+-----+-----+ 2820

ACACACATCTCCTCAAATATCCCTTTCCAGTGTGACTCGAATGCTGTCGAATCGA  
 2821 -----+-----+-----+-----+-----+-----+ 2880  
 V D S N A V E F E  
 100

GTGTCCAATGTCACCGCAAGCCATCGTCGGAGCCGCGCATTGAGCCCCGGCTACAC  
 2881 -----+-----+-----+-----+-----+-----+ 2940  
 C P M S P A S H R R S R A L S P A G Y T  
 110 120

TTCACCGACCCGAGTTCACCGTACAGCGTCTTCAGTGTCAATTCACTTCTTATCA  
 2941 -----+-----+-----+-----+-----+-----+ 3000  
 S P T R V H R D S V S S V S S F T S Y Q  
 130 140

GGATATCTACTCAAGAGCAAGATCTCGTCTCGATCGCGTGCACCCATTCACTCGGATCG  
 3001 -----+-----+-----+-----+-----+-----+ 3060  
 D I Y S R A R S R S R A L H S S D R  
 150 160

| Intron 3  
 ACACAATTATTCACTCCTCCAGTCAACGCATTCCCAGCCAACCTTGATGTTGATGCG  
 3061 -----+-----+-----+-----+-----+-----+ 3120  
 H N Y S S P P V N A F P S Q P S  
 170



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## FIG. 4D

### Repeat 1

3121 AACACTAAATTCTGAGAATGCGCATTACTCAACATATTCGACGGCAAATATCTCGTAGC 3180

3181 GAAAAATACAGTAACCCTTAAATGACTATTGTAGTGTGATTACGGGCTGATTTCG 3240

3241 AAACGAATATATGCTCGAACATTGTGACAACGAATTAAATTGTCATTTGTGTTTCTT 3300

### Repeat 1

3301 TTGATATTTGATCAATTAATAATTATTCGTAAACAGACACCAGCGCTACAGTACT 3360

3361 CTTTTAAAGAGTTACAGTAGTTTCGCTTCAAGATATTGAAAAGAATTAAACATT 3420

3421 TGAAAAAAATCATCTAACATGTGCCAAACGCTTTTCAAGTTCGCAGATTTTG 3480

### Repeat 2

3481 TTTTTTCATTCAAGATATGCTTATTAACACATATAATTATCATTATGTGAATTCTTG 3540

3541 TAGAAATTTGGGCTTTCTAGTATGCTCTACTTTGAAATTGCTAACGAAAAAA 3600

3601 TCATGTGGTTGTTCATATGAATGACGAAAAATAGCAATTATATATTTCCCCTAT 3660

3661 TCATGTTGTGCAGAAAAATAGTAAAAAGCGCATGCATTTGACATTACATCGA 3720

3721 ACGACAGCTCACTCACATGCTGAAGACGAGAGACGCGGAGAAATACACACATCTTCT 3780

### Repeat 2

3781 GCGTCTCTCGTCTCAGCATGTGAAATGGATCTCGGTGATGTAAAAAAATGTCGAAATA 3840

3841 ATGTAATAATGCATGCGTTTTACACTTTCTGCACAAATGAATAGGGGAAATGT 3900

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## FIG. 4E

ATTTAAACATTTTGATTTCAACATCACATGATTAACCCATTATTTTCGTT 3960  
 3901 -----+-----+-----+-----+-----+-----+-----+  
 GAGCAACTAAAAAGTAGAGAATATTAGAGCGAAAACCAAAATTCTCAAGATATTACC 4020  
 3961 -----+-----+-----+-----+-----+-----+-----+  
 TTTATTGATAATTATAGATGTTAATAAGCATATCTGAATGAAAGTCAGCAAAATATGT 4080  
 4021 -----+-----+-----+-----+-----+-----+-----+  
 GCGAAAACACCTGAAAAAAATCAAAATTCTGCAGAAAATTGAGAAAATGCATTAAAATACA 4140  
 4081 -----+-----+-----+-----+-----+-----+-----+  
 TTTTGCACTTCTACATCACATGAATGTAGAAAATTAAAAGGGAAATCAAATTCTA 4200  
 4141 -----+-----+-----+-----+-----+-----+-----+  
 GAGGATATAATTGAATGAAACATTGCGAAATTAAATGTGCGAACGTCAAAAGAGGA 4260  
 4201 -----+-----+-----+-----+-----+-----+-----+  
 |  
 AATTTGGGTATCAAATCGATCCTAAAACCAACACATTTCAGCATCCGCCAATCTTCAT 4320  
 4261 -----+-----+-----+-----+-----+-----+-----+  
 S A N S S F  
 180  
 TCACCGGATGCTCTCTCTCGGATACAGTTCAAGTCGAATCGCTCATTAGCAAGCTT 4380  
 4321 -----+-----+-----+-----+-----+-----+-----+  
 T G C S S L G Y S S S R N R S F S K A S  
 190 200  
 CTGGACCAACTCAATACATATTCCATGAAGAGGATATGAACATTGTCGATGCACCAACCA 4440  
 4380 -----+-----+-----+-----+-----+-----+  
 G P T Q Y I F H E E D M N F V D A P T I  
 210 220  
 TAAGCCGTGTTTCGACGAGAAAACCATGTACAGAAACTTCTCGAGTCCTCGTGGATGT 4500  
 4441 -----+-----+-----+-----+-----+-----+  
 S R V F D E K T M Y R N F S S P R G M C  
 230 240  
 GCCTCATCATAATAATGAACACTTGGAGCAGATGCCAACACGGAAATGGTACCAAGGCCG 4560  
 4501 -----+-----+-----+-----+-----+-----+  
 L I I N N E H F E Q M P T R N G T K A D  
 250 260  
 ACAAGGACAATCTTACCAATTGTTAGATGCATGGCTATACGGTATTTGCAAGGACA 4620  
 4561 -----+-----+-----+-----+-----+-----+  
 K D N L T N L F R C M G Y T V I C K D N  
 270 280  
 | Intron 4  
 ATCTGACGGGAAGGGTACGGCGAAATTATATTACCCAAACCGCGAAATTGCCATTTGCG 4680  
 4621 -----+-----+-----+-----+-----+-----+  
 L T G R



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## FIG. 4F

### Repeat 3

	----->	
4681	CCGAAAATGTGGCGCCCGGTCTGACACGACAATTGTGTTAAATGCAAAATGTATAAT	4740
4741	TTTGCAAAAACAAAATTTGAACCTTCCGCAGAAATGATTTACCTAGTTTCGAAATTTC	4800
4801	GTTTTTCCGGCTACATTATGTGTTTTCTTAGTTCTATAATATTTGATGTAAAAA	4860
4861	ACCGTTGTAAATTTCAGACAATTTCAGCATACAAAACCTGATAGCACGAAATCAATT	4920
4921	TTCTGAATTTCAAAATTATCCAAAATGCACAATTAAAATTGTGAAATTGGCAAAC	4980
4981	GGTGTTCATATGAAATGTATTTAAAAACTTAAACCCACTCCGAAAAGCAATAA	5040
5041	AAATCAAAACACGTACAATTCAAATTCAAAGTTATTCATCCGATTTGTTATTTG	5100
5101	CAAAATTGAAAAAAATCATGAAGGATTAGAAAAGTTTATAACATTTCTAGATT	5160
5161	TCAAAATTTTTTAACAAATCGAGAAAAGAGAATGAAAATCGATTTAAAAATATCC	5220

### Repeat 3

5221	ACAGCTCGAGAGTTGAAATTACAGTACTCCTAAAGCGCACACCCATTGCATTGG	5280
5281	ACCAAAAATTGCGTGTGAGACCAGGTACCGTAGTTTGTGCAAAATTGCACCAT	5340
5341	TGGACAATAACCTCTTAATCACCAAAAGTAAATTGAAATCTCGAAAAGCCAAA	5400
5401	ATTCAAAAAAAAGTCGAATTGATTTTTGGTTTTGGTCCCACCAAAACCAAA	5460
5461	AAATCAATTCTGCAAAATACCAAAAGAACCGAAAAATTCCCAGCCTGTCCT	5520
5521	AATGTAAACTGATATTAATTCCAGGAATGCTCTGACAATTGAGACTTGCCAAAC	5580

G M L L T I R D F A K H  
290 300

5581	ACGAATCACGGAGATTCTGCGATACTCGTGATTCTATCACACGGAGAAGAGAATGTGA	5640
	E S H G D S A I L V I L S H G E E N V I	
	310 320	

5641	TTATTGGAGTTGATGATACCGATTAGTACACACGAGATATGATCTTCTAACCGCGG	5700
	I G V D D I P I S T H E I Y D L L N A A	
	330 340	



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## FIG. 4G

A (n2433)  
| | Intron 5

CAAATGCTCCCCGTCTGGCGAATAAGCCGAAATCGTTTGTGCAGGCTTGTCAAGGGCG  
5701 -----+-----+-----+-----+-----+-----+-----+ 5760  
N A P R L A N K P K I V F V Q A C R G E  
350 360

GTTCGTTTTTATTTAATTTAATAAAATATTTAAATAATTCACTTCAGAACGTC  
5761 -----+-----+-----+-----+-----+-----+-----+ 5820  
R R

GTGACAAATGGATTCCCAGTCTGGATTCTGTCGACGGAGTTCTGCATTCTTCGTG  
5821 -----+-----+-----+-----+-----+-----+-----+ 5880  
D N G F P V L D S V D G V P A F L R R G  
370 380

T (n1165)  
|  
GATGGGACAATCGAGACGGGCCATTGTTCAATTTCTTGATGTGTGCAGGCCGCAAGTC  
5881 -----+-----+-----+-----+-----+-----+-----+ 5940  
W D N R D G P L F N F L G C V R P Q V Q  
390 400

| Intron 6  
AGGTTGCAATTTAATTCTTGAATGAGAATATTCTTCAAAAATCTAAAATAGATTTT  
5941 -----+-----+-----+-----+-----+-----+-----+ 6000  
ATTCCAGAAAGTCCCATCGAAAAATTGCGATATAATTACGAAATTGTGATAAAATGAC  
6001 -----+-----+-----+-----+-----+-----+-----+ 6060

Repeat 4  
-----  
AAACCAATCAGCATCGTCGATCTCCGCCACTTCATCGGATTGGTTGAAAGTGGCGGA  
6061 -----+-----+-----+-----+-----+-----+-----+ 6120

----->  
GTGAATTGCTGATTGGTCGCAGTTTCAGTTAGAGGAAATTAAAAATCGCCTTTCGA  
6121 -----+-----+-----+-----+-----+-----+-----+ 6180  
AAATTAAAAATTGATTTTCATTTTCGAAAAATTCCGATTATTTATATTCTTT  
6181 -----+-----+-----+-----+-----+-----+-----+ 6240

A (n717)  
|  
GGAGCGAAAGCCCCGTCTGAAACATTTAAATGATAATTAATAATTGGCAGCAA  
6241 -----+-----+-----+-----+-----+-----+-----+ 6300  
Q

T (n1949)  
|  
GTGTGGAGAAAGAAGCCGAGCCAAGCTGACATTCTGATTGATCGAACGACAGCTCAA  
6301 -----+-----+-----+-----+-----+-----+-----+ 6360  
V W R K K P S Q A D I L I R Y A T T A Q  
410 420

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## FIG. 4H

### A (n1286)

TATGTTCGTGGAGAACAGTGCTCGTGGATCATGGTCATTCAAGCCGTCTGTGAAGTG  
 6361 -----+-----+-----+-----+-----+-----+-----+ 6420  
 Y V S W R N S A R G S W F I Q A V C E V  
 430 440

### T (n1129, n1164)

TTCTCGACACACGAAAGGATATGGATGTTGAGCTGCTGACTGAAGTCATAAGAAG  
 6421 -----+-----+-----+-----+-----+-----+ 6480  
 F S T H A K D M D V V E L L T E V N K K  
 450 460

### T (n2430)

A (n2426)  
 6481 -----+-----+-----+-----+-----+-----+ 6540  
 GTCGCTTGTGGATTCAGACATCACAGGGATCGAATATTTGAAACAGATGCCAGAGGTA  
 V A C G F Q T S Q G S N I L K Q M P E  
 470 480

### Repeat 5

CTTGAAACAAACAATGCATGTCTAACTTTAAGGACACAGAAAAATAGGCAGAGGCTCCT  
 6541 -----+-----+-----+-----+-----+-----+ 6600

----->

TTTGCAAGCCTGCCGCGTCAACCTAGAATTTAGTTTAGCTAAAATGATTGATT  
 6601 -----+-----+-----+-----+-----+-----+ 6660  
 GAATATTTATGCTAATTTTTGCGTTAATTTGAAATAGTCACTATTTATCGGGTT  
 6661 -----+-----+-----+-----+-----+-----+ 6720  
 CCAGTAAAAATGTTATTAGCCATTGGATTTACTGAAAACGAAAATTGTAGTTTC  
 6721 -----+-----+-----+-----+-----+-----+ 6780  
 AACGAAATTATCGATTTAAATGAAAAAAAAAGCGAAAATTACATCAACCATA  
 6781 -----+-----+-----+-----+-----+-----+ 6840  
 GCATTTAAGCCAAAATTGTTAACTCATTAAAAATTAAATTCAAAGTTGCCACGAGTATT  
 6841 -----+-----+-----+-----+-----+-----+ 6900

### Repeat 5

<-----

ACACGGTTGGCGCGCGCAAGTTGCAAAACGACGCTCCGCCCTTTCTGTGCCGCTT  
 6901 -----+-----+-----+-----+-----+-----+ 6960

### T (n1163)

-----  
 GAAAACAAGGGATCGGTTAGATTTCCCCAAAATTAAATTAAATTTCAGATGACATC  
 6961 -----+-----+-----+-----+-----+-----+ 7020  
 M T S

CCGCCTGCTCAAAAGTTCTACTTTGCCGGAAGCAGAAACTCTGCCGTCTAAATTC  
 7021 -----+-----+-----+-----+-----+-----+ 7080  
 R L L K K F Y F W P E A R N S A V \*  
 490 500

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## FIG. 4I

ACTCGTGATTCAATTGCCAATTGATAATTGTCTGTATCTTCTCCCCAGTTCTTTGC  
7081 -----+-----+-----+-----+-----+-----+-----+ 7140  
CCAATTAGTTAAAACCATGTGTATATTGTTATCCTATACTCATTCACTTATCATTCT  
7141 -----+-----+-----+-----+-----+-----+-----+ 7200  
ATCATTCTCTTCCCATTTCACACATTCCATTCTACGATAATCTAAAATTATGAC  
7201 -----+-----+-----+-----+-----+-----+-----+ 7260  
GTTTGTGTCTCGAACGCATAATAATTAACTCGTTTGAAATTGATTAGTTGTTGT  
7261 -----+-----+-----+-----+-----+-----+-----+ 7320  
GCCAGTATATATGTATGTACTATGCTTCTATCAACAAAATAGTTCATAGATCATCACC  
7321 -----+-----+-----+-----+-----+-----+-----+ 7380  
CCAACCCCACCAACCTACCGTACCATATTCAATTGGCCGGGAATCAATTGATTAAATT  
7381 -----+-----+-----+-----+-----+-----+-----+ 7440  
TTAACCTATTTTCGCCACAAAAATCTAATATTGAATTAACGAATAGCATTCCCATC  
7441 -----+-----+-----+-----+-----+-----+-----+ 7500  
TCTCCCGTGCCGGAAATGCCCTCCGGCCTTTAAAGTTCGAACATTGGCAATTATGTAT  
7501 -----+-----+-----+-----+-----+-----+-----+ 7560  
AAATTGTAGGTCCCCCCCATCATTCCGCCATCATCTCAAATTGCATTCTTTTCG  
7561 -----+-----+-----+-----+-----+-----+-----+ 7620  
CCGTGATATCCCGATTCTGGTCAGCAAAGATCT  
7621 -----+-----+-----+-----+-----+-----+-----+ 7653

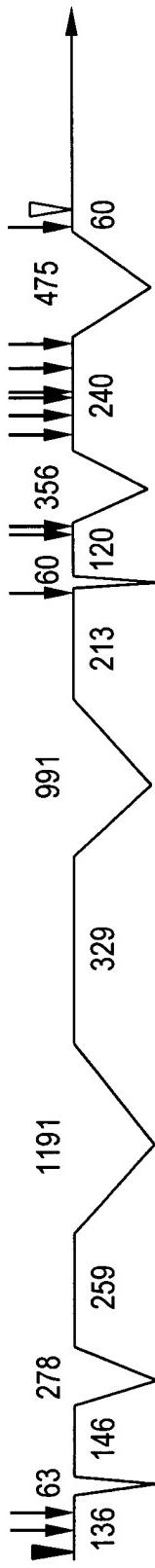
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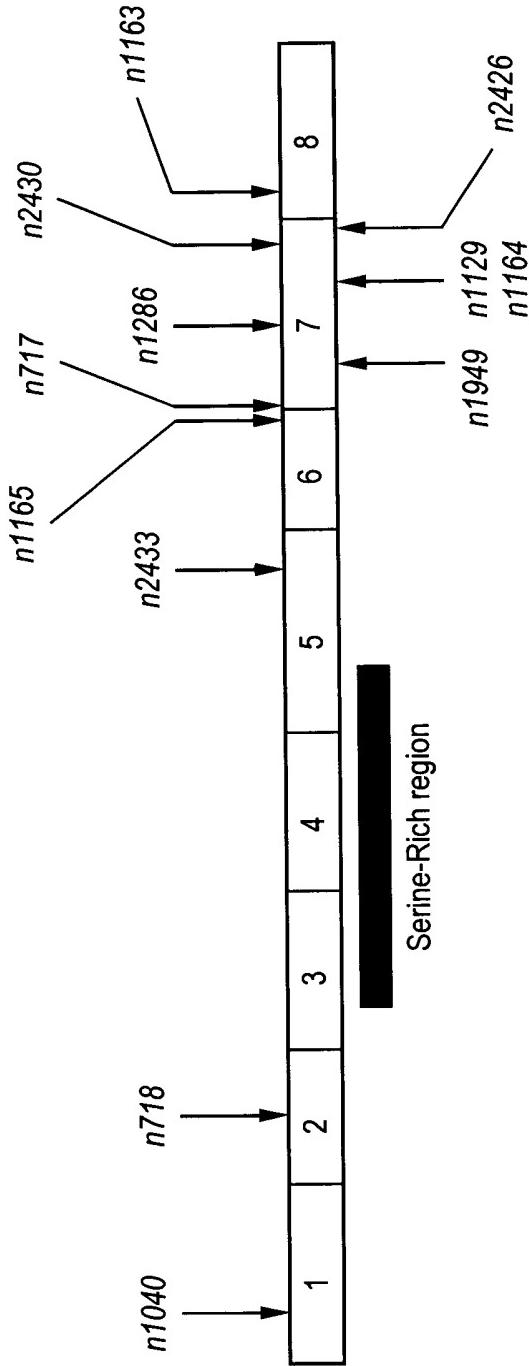
FIG. 5A



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## FIG. 5B

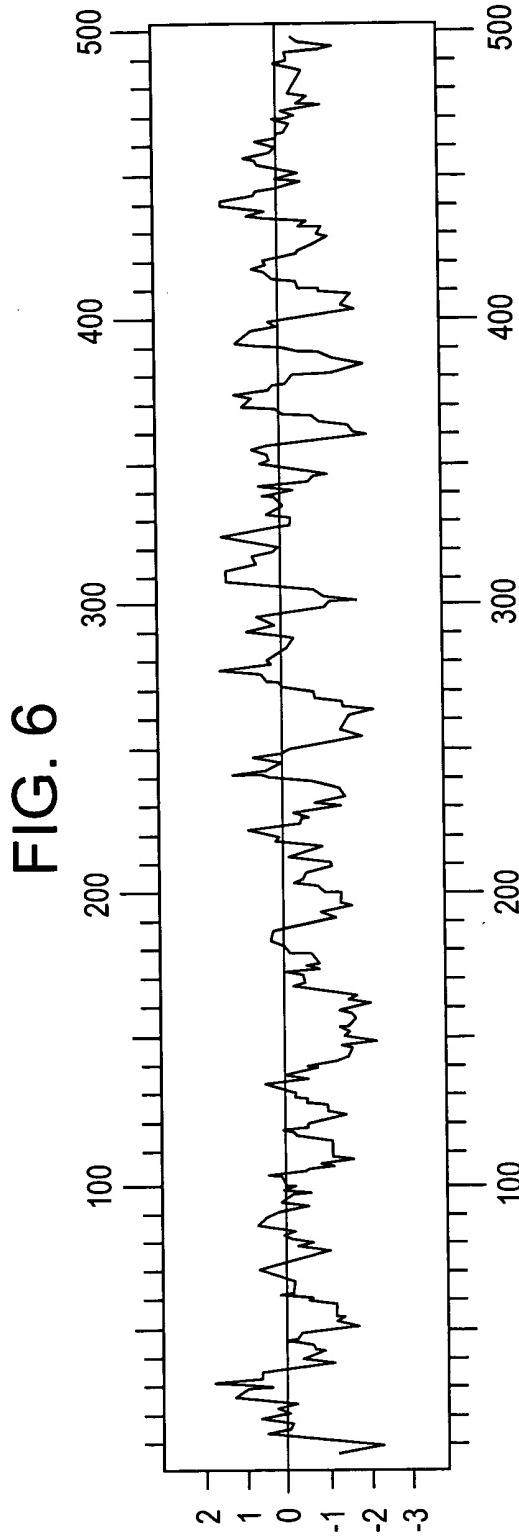
*ced-3* Mutations are Clustered





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## FIG. 7

**Lines**

1	01 MMRQDRRLERNIMMFSSHLKVDEILEVLIAKQVLNSDNGDMINSCGTV 50
2	.....W.....LE...K.QA.L.D.....V....R.E
3	.....TVS.SLI..R.....M.....
1	51 REKRREIVKAVQRPGDVAFDAFYDALRSTGHEGLAEVLEPLARSVDNAV 100
2	.....DNEK.....R..E.....D...ND..D..M..S.P.....P.
3	
1	101 EFECPMSPASHRRSRALSPAGYTSPTRVHRDSVSSVSSFTS YQDIYSRA 149
2	PM.....S.....P.A.....I.....T...V....
3	S
1	150 RSRSR SRALHSSDRHNYSSPPVNAFPSQPSSANSSFTGCSSLGYSSSRN 198
2	.....S..S..P.Q.....M_AA_TS.....A.....
3	T.....P.T.....V..S..S.Q..A.....S.....T
1	199 RSFSKASGPTQYIFHEEDMFVDAPTISRVFDEKTMYRNFSSPRGMCLI 247
2	.....T.AQS.....Y.....H.....L...
3	.....Y....AHS.....Y.....H.....T...L...
1	248 INNEHFEQMPTRNGTKADKDNLTNLFRCMGYTICKDNLTGRGMLLTIRD 297
2	.....I.....E..S...S
3	.....P...IS.....I.H.....M.....
1	298 FAKHESHGDSAILVILSHGEENVIIIGVDDIPISTHEIYDLLNAANAPRLA 347
2	.....GRNDM.....VSVNV.....
3	.....N.T.....VSVNV....X.....
1	348 NPKKIVFVQACRGERRDNGFPVLDSDGVPAFLRRGWDNRDGPLNFLGC 397
2	.....L.....SLI.....
3	.....L.....V.....LI.....KG.....
1	398 VRPQVQQVWRKKPSQADILIRYATTAQYVSWRNSARGSWFIQAVCEVFST 447
2	.....M.A.....L
3	.....A.....A.....L
1	448 HAKDMVVELLTEVNKKVACGFQTSQGSNILKQMPEMTSRLKKFYFWPE 497
2	.....L.....
3	.....A.....L.....
1	498 ARN SAV 503
2	DRG.....
3	.....D..RS...

Line 1 *C. elegans*

Line 2 *C. briggsae*

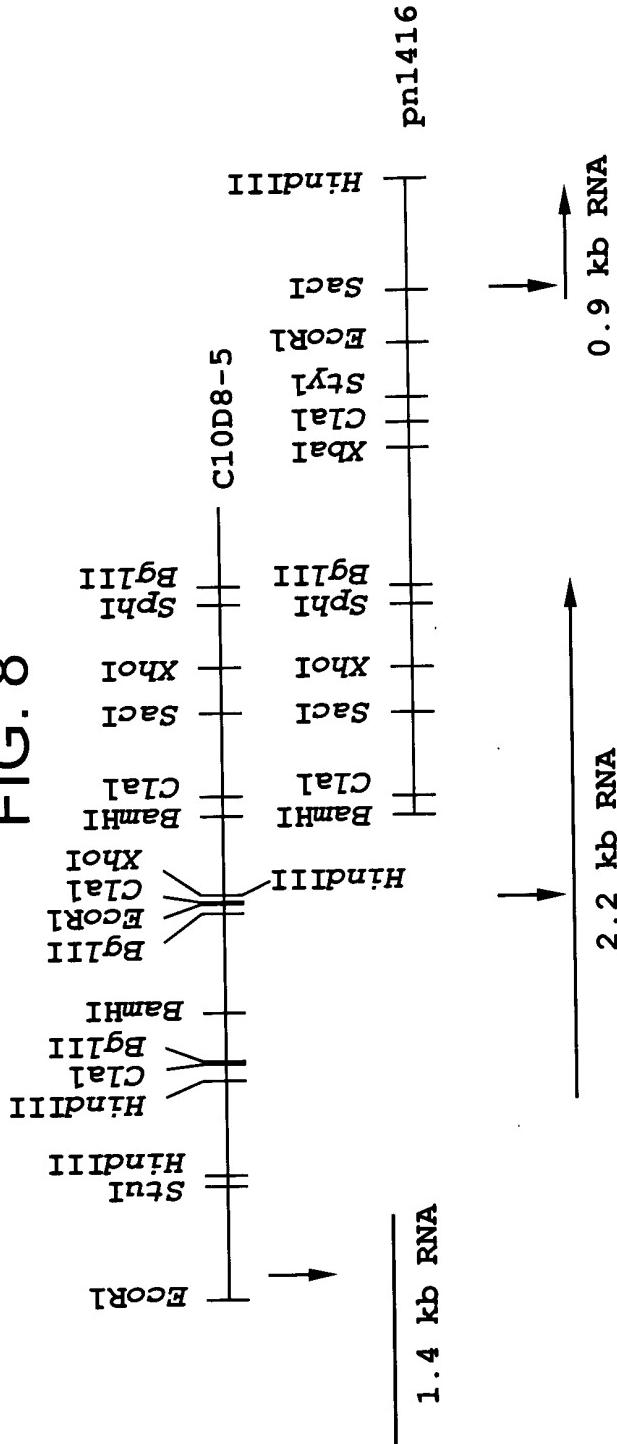
Line 3 *C. vulgaris*

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## FIG. 9



O P E  
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## FIG. 10

Summary of the experiments to localize *ced-3* gene within C40D1

